REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.113, is respectfully requested.

The Examiner requested that claims 3-5, 17, 22-24 and 28-40 be canceled in light of the Board's decision dated August 27, 2008. Applicants, however, respectfully decline the Examiner's request should further appeals be in order.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 14, 18, 19 and 25-27 stand rejected under 35 U.S.C. § 103(a) as purportedly obvious in view of Ebert (U.S. Pat. No 5,662,925), Cormier (U.S. Pat. No. 6,203,817) and Ke (U.S. Pat. No. 6,323,232). This rejection is respectfully traversed.

In the present action, the Examiner reasserted the Board's reasons for rejection in an attempt to show all of the claim elements were present in the prior art and that the claimed invention would be obvious to one of ordinary skill in the art. These assertions, however, are based on a mischaracterization and oversimplification of the publications cited and the false presumption that compounds with similar pharmacological activities have similar chemical properties.

For example, after acknowledging that both the '952 and '817 patents do not disclose lasofoxifene (*see* Final Office Action dated 12/12/08, page 3, first and second paragraphs), the Examiner attempted to combine a publication that lists lasofoxifene in the last two sentences of the document (*see* '232 patent claims 1 and 2 at col. 40, lines 48-55) in order to demonstrate a

transdermal formulation that would render the pending claims obvious. The argument for combining these publications, however, is flawed because it mischaracterizes the formulation in the '232 patent that the Examiner relies on as demonstrating a transdermal drug delivery device. The '232 publication only discloses a parenteral solution for topical application. A formulation fundamentally different than the complex transdermal delivery device claimed. For example, at column 37, lines 49-52 the '232 specification states:

> For purposes of transdermal (e.g., topical) administration, dilute sterile, aqueous or partially aqueous solutions (usually in about 0.1% to 5% concentration), otherwise similar to the above parenteral solutions, are prepared.

The differences between this formulation and the drug delivery device claimed are innumerable as outlined in Dr. Coop's declaration filed on October 27, 2008. The most significant being that the instant claims are directed to a device and the '232 patent merely discloses a parenteral solution for topical administration. To this end, the Examiner failed to explain how one of ordinary skill in the art could equate a parenteral solution with a transdermal drug delivery device that provides controlled drug delivery over an extended period of time given the complexities that are involved in such a formulation.

Instead, the Examiner seems to gloss over these complexities and asserts that one of ordinary skill in the art would just combine Cormier and Ke with the transdermal device in Ebert to render the invention set forth in claims 14, 18, 19 and 25-27 obvious based on the assertion that all three publications contain a reference to antiestrogenic drugs.

This flawed assertion fails to take into account the differences in chemical properties dictated by the functional groups among the antiestrogenic compounds and how these properties dictate their formulation. In addition, the Examiner's argument is based on the false presumption

that drugs of the same pharmacological class possess similar chemical properties that would allow their interchangeability in transdermal formulations.

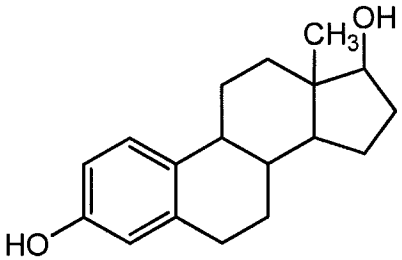
It is a well-established principle of patent law that compounds of similar *structure* are presumed to have similar properties. *See, In re Dillon*, 919 F.2d 688, 692-693; 16 U.S.P.Q. 2d 1897, 1901 (Fed. Cir. 1990). However, there is *no* legal basis for presuming the converse, *i.e.*, that compounds with similar pharmacological activities necessarily have similar chemical structures or characteristics. In fact, the opposite is true. The court has stated that "we would observe that the mere inclusion of several compounds in a list of compounds...does not necessarily establish that each of those compounds is equivalent to the others for all purposes." *See, e.g., In re Jezl*, 396 F.2d 1009, 1012; 158 U.S.P.Q. 98, 99-100 (CCPA 1968).

It is well known in the art that a compound's pharmacological classification is based on the behavior a compound exhibits in the human body and not on its chemical make-up. For example, antiestrogenic compounds such as lasofoxifene have a single characteristic in common - the fact that they work against the effect of estrogen *in vivo*. It is only because of this activity that they are listed together under the pharmacologic class of antiestrogenic compounds. The Examiner's assertion, however, that the use of lasofoxifene in the claimed device would be obvious because it is an antiestrogenic agent and a functional equivalent of the other compounds listed is one that is not supported by the case law. The court has stated that "[e]xpedients which are functionally equivalent to each other are not necessarily obvious in view of one another." *See, e.g., In re Scott*, 323 F.2d 1016, 1019; 139 U.S.P.Q. 297, 299 (CCPA 1963). And, in this case, the difference in chemical makeup of the compounds cited by the Examiner clearly demonstrate that they are not obvious in view of one another.

In fact, the Examiner's own statements in the instant office action demonstrate that he has not taken into account the differences between the compounds asserted to be "functional equivalents." For example, the Examiner stated in the first full paragraph on page 4 of the office action dated December 12, 2008 that:

> It would have been obvious to a person of ordinary skill in the art to combine the device of the '925 patent with the transdermal administration of lasofoxifene shown in the '817 patent and the '232 patents since Ebert discloses that the device is useful for the administration of a variety of agents in **including estradiols** (col. 4, lin. [sic] 20). [emphasis added]

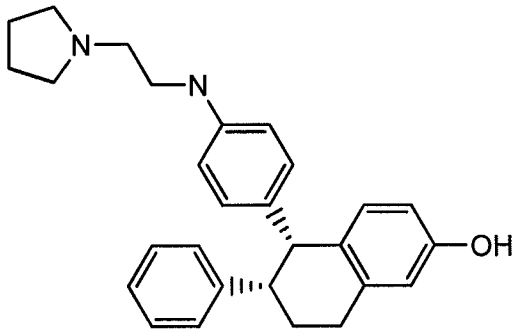
The Examiner's inclusion of lasofoxifene with a discussion of estradiols demonstrates that he has oversimplified the difficulty in formulating the transdermal formulation of the instant claims as outlined by Dr. Coop. Estradiols possess the following chemical structure that, in turn, possesses unique chemical properties:



Estradiol [1]

[1] See Hawley's Condensed Chemical Dictionary (Eleventh Edition) 1987.

The reference to estradiols in the '925 patent does not refer to or suggest compounds such as lasofoxifene having the following very different structure:



Lasofoxifene

The differences in structure among the compounds listed in the publications cited must be taken into account when formulating transdermal delivery devices since they introduce unpredictability. However, this unpredictability is precisely what the Examiner failed to account for in his assertion that those of ordinary skill in the art would combine Cormier, Ke and Ebert with a reasonable expectation of success to yield the invention set forth in claims 14, 18, 19 and 25-27.

As set forth in the declaration of Dr. Andrew Coop, the chemical makeup and functional groups possessed by the compounds described in Cormier (that include tamoxifen and raloxifene) are significantly different from those of lasofoxifene. Dr. Coop also notes that the chemical makeup and functional groups of the antiestrogenic compounds listed in Ke (droloxifene and idoxifene) are significantly different from those of lasofoxifene. The very fact that these functional groups differ is the sound reasoning demonstrating why chemical structure affects properties such as the stability of the active ingredient, the stability of the adjuvant in combination with the active ingredient, the phase distribution of the compound within a matrix, the release of the compound from the matrix, pH and bioavailability. All of these differing

physical and chemical properties, however, were not accounted for by the Examiner in asserting the obviousness rejection.

Thus, as Dr. Coop notes, the fact that several assumptions must be made based on the unpredictable components would not lead one of ordinary skill in the art to conclude that lasofoxifene could be successfully and predictably used in a transdermal drug delivery device based on their established functions.

With regard to the declaration submitted under 37 C.F.R. § 1.132, the Examiner stated that Dr. Coop's sworn statement was "an opinion of an unrelated party" that argues the same points set forth in previous responses. In response, Applicants respectfully request the Examiner to reconsider the evidence of nonobviousness and address each of the points raised by Dr. Coop as they demonstrate how the currently claimed invention would not be obvious to those of ordinary skill in the art. Applicants submit that by addressing each of the points in the declaration, it will be evident to the Examiner that the combination of publications cited does not suggest the invention claimed by Applicants.

Accordingly, it is submitted that the presently claimed invention is not obvious over the cited publications in view of the multitude of variables required to be considered in formulating a transdermal device for the delivery of lasofoxifene. Because of that unpredictability, the presently claimed invention does not arise from the predictable use of prior art elements based on their established functions. The extent of this unpredictability would dissuade one of skill in the art from combining the references to claim the invention as the Applicants have. For all these reasons, it is respectfully requested that this rejection be withdrawn.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order and such action is respectfully requested.

In the event that there are any questions relating to this Amendment or to the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (202) 373-6000 so that prosecution of the application may be expedited.

The Director is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-4047.

Respectfully submitted,

BINGHAM MCCUTCHEN, LLP

Date: February 12, 2009

By: _____
Matthew L. Fedowitz
Registration No. 61,386

BINGHAM MCCUTCHEN, LLP
2020 K Street, NW
Washington, DC 20006
Telephone: (202) 373-6000
Facsimile: (202) 373-6001